AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-12 (Canceled)

Claim 13 (Concurrently Amended): A method for reduction of a substrate with thioredoxin reductase, comprising combining the thioredoxin reductase, the substrate and NADPH in an in vitro composition, wherein the composition does not include insulin, under conditions to reduce the substrate, the substrate comprising a substance selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:

$$\begin{array}{c|c}
R^1 & Y \\
N & (CH_2)_n - R^3 \\
R^5 & \\
R^4 & (1)
\end{array}$$

$$\begin{bmatrix} R^1 & Y & (CH_2)_n - R^3 \\ R^2 & Se & \end{bmatrix}$$
 (1')

wherein R^1 and R^2 independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a C_1 - C_6 alkyl group, or a C_1 - C_6 alkoxyl group, or R^1 and R^2 may combine together to represent methylenedioxy group; R^3 represents an aryl group, an aromatic heterocyclic group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; R^4 represents a hydrogen atom, a hydroxyl group, a -S-glutathione group, a -S- α -amino acid group, or an aralkyl group whose aryl moiety may be substituted with one or more substituents; R^5 represents a hydrogen atom or a C_1 - C_6 alkyl group, or R^4 and R^5 may combine together to represent single bond; Y represents oxygen atom or sulfur atom; n represents an integer of from 0 to 5; and the selenium atom may be oxidized.

Claim 14 (Previously Presented): The method according to claim 13 wherein the substrate comprises a substance selected from the group consisting of 2-phenyl-1,2-benziso-selenazol-3(2H)-one or a ring-opened form thereof and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof.

Claim 15 (Concurrently Amended): A method of enhancing peroxidase activity of thioredoxin reductase, comprising combining NAPDH, thioredoxin reductase, thioredoxin and a substrate in an in vitro composition, wherein the composition does not include insulin, under conditions to enhance peroxidase activity of thioredoxin reductase, the substrate comprising a substance selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:

$$\begin{array}{c|c}
R^{1} & Y \\
N & (CH_{2})_{n} - R^{3} \\
R^{2} & Se \\
R^{4} & R^{4}
\end{array}$$
(1)

$$\begin{bmatrix} R^1 & Y & (CH_2)_n - R^3 \\ R^2 & Se & R^5 \end{bmatrix}$$
 (1')

wherein R^1 and R^2 independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a C_1 - C_6 alkyl group, or a C_1 - C_6 alkoxyl group, or R^1 and R^2 may combine together to represent methylenedioxy group; R^3 represents an aryl group, an aromatic heterocyclic group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; R^4 represents a hydrogen atom, a hydroxyl group, a -S-glutathione group, a -S- α -amino acid group, or an aralkyl group whose aryl moiety may be substituted with one or more substituents; R^5 represents a hydrogen atom or a C_1 - C_6 alkyl group, or R^4 and R^5 may combine together to represent single bond; Y represents oxygen atom or sulfur atom; R^4 and R^5 may combine together to represent single bond; Y represents oxygen atom or sulfur atom; R^4 and R^5 may combine together to represent single bond; Y represents oxygen atom or sulfur atom;

Claim 16 (Previously Presented): The method according to claim 15 wherein the substrate comprises a substance selected from the group consisting of 2-phenyl-1,2 benzisoselenazol-3(2H)-one or a ring-opened form thereof and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof.

Claim 17 (Concurrently Amended): A method of oxidizing reduced thioredoxin by a substrate, the method comprising combining reduced thioredoxin and a substrate in an *in vitro* composition, wherein the composition does not include insulin, under conditions to oxidize the reduced thioredoxin with the substrate, the substrate comprising a substance selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:

$$\begin{array}{c|c}
R^{1} & Y & (CH_{2})_{n} - R^{3} \\
 & R^{2} & R^{5} \\
 & R^{4} & (1)
\end{array}$$

$$\begin{bmatrix} R^1 & Y & (CH_2)_n - R^3 \\ R^2 & R^5 \end{bmatrix}$$
 (1')

wherein R^1 and R^2 independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a C_1 - C_6 alkyl group, or a C_1 - C_6 alkoxyl group, or R^1 and R^2 may combine together to represent methylenedioxy group; R^3 represents an aryl group, an aromatic heterocyclic $\{P21480\ 00774850.DOC\}$

group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; R^4 represents a hydrogen atom, a hydroxyl group, a -S-glutathione group, a -S- α -amino acid group, or an aralkyl group whose aryl moiety may be substituted with one or more substituents; R^5 represents a hydrogen atom or a C_1 - C_6 alkyl group, or R^4 and R^5 may combine together to represent single bond; Y represents oxygen atom or sulfur atom; n represents an integer of from 0 to 5; and the selenium atom may be oxidized.

Claim 18 (Concurrently Amended): A method for reducing a peroxide comprising combining thioredoxin, thioredoxin reductase, NAPDH and a substrate in an *in vitro* composition, wherein the composition does not include insulin, under conditions to reduce the peroxide, the substrate comprising a substance selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:

$$\begin{array}{c|c}
R^1 & Y \\
N & (CH_2)_n - R^3 \\
R^5 & \\
R^4 & (1)
\end{array}$$

$$\begin{bmatrix} R^1 & Y & (CH_2)_n - R^3 \\ R^2 & Se & R^5 \end{bmatrix}$$
 (1')

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wherein R^1 and R^2 independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a C_1 - C_6 alkyl group, or a C_1 - C_6 alkoxyl group, or R^1 and R^2 may combine together to represent methylenedioxy group; R^3 represents an aryl group, an aromatic heterocyclic group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; R^4 represents a hydrogen atom, a hydroxyl group, a -S-glutathione group, a -S- α -amino acid group, or an aralkyl group whose aryl moiety may be substituted with one or more substituents; R^5 represents a hydrogen atom or a C_1 - C_6 alkyl group, or R^4 and R^5 may combine together to represent single bond; Y represents oxygen atom or sulfur atom; n represents an integer of from 0 to 5; and the selenium atom may be oxidized.

Claim 19 (Concurrently Amended): A method of preventing peroxidation of a substance comprising combining thioredoxin, thioredoxin reductase and NADPH with a substrate <u>in an in vitro</u> composition, wherein the composition does not include insulin, under conditions to prevent peroxidation of the substance, the substrate being selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:

$$\begin{array}{c|c}
R^1 & Y \\
N & (CH_2)_n - R^3 \\
R^2 & Se \\
R^4 & (1)
\end{array}$$

$$\begin{bmatrix} R^1 & Y & (CH_2)_n - R^3 \\ R^2 & Se & R^5 \end{bmatrix}$$
 (1')

wherein R^1 and R^2 independently represent a hydrogen atom, a halogen atom, a trifluoromethyl group, a nitro group, a C_1 - C_6 alkyl group, or a C_1 - C_6 alkoxyl group, or R^1 and R^2 may combine together to represent methylenedioxy group; R^3 represents an aryl group, an aromatic heterocyclic group, a 5- to 7-membered cycloalkyl group, or a 5- to 7-membered cycloalkenyl group, and the aryl group, the aromatic heterocyclic group, the cycloalkyl group, and the cycloalkenyl group may be substituted with one or more substituents; R^4 represents a hydrogen atom, a hydroxyl group, a -S-glutathione group, a -S- α -amino acid group, or an aralkyl group whose aryl moiety may be substituted with one or more substituents; R^5 represents a hydrogen atom or a C_1 - C_6 alkyl group, or R^4 and R^5 may combine together to represent single bond; Y represents oxygen atom or sulfur atom; R^4 and R^5 may combine together to represent single bond; Y represents oxygen atom or sulfur atom; R^4 and R^5 may combine together to represent single bond; Y represents oxygen atom or sulfur atom;

Claims 20-25 (Canceled)

Claim 26 (Previously Presented): The method according to claim 17 wherein the substrate comprises a substance selected from the group consisting of 2-phenyl-1,2-benziso-selenazol-3(2H)-one or a ring-opened form thereof and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof.

Claim 27 (Previously Presented): The method according to claim 18 wherein the substrate comprises a substance selected from the group consisting of 2-phenyl-1,2-benziso-selenazol-3(2H)-one or a ring-opened form thereof and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof.

Claim 28 (Previously Presented): The method according to claim 19 wherein the substrate comprises a substance selected from the group consisting of 2-phenyl-1,2-benziso-selenazol-3(2H)-one or a ring-opened form thereof and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof.